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(54) **Mixers**

(57) A mixer for supplying a sterilizing medium to an isolator, comprises an elongate mixing chamber (11) having at one end an entrance (21) through which gas (e.g. air) may be fed in so as to swirl around and along the chamber to the other end, where there is an exit (27) through which the gas can leave; and an atomiser (14) in the chamber adjacent the entrance to which is fed a sterilizing liquid such that the spray produced is drawn into the swirling gas. The chamber may be provided on its exterior with an electric heating tape (25) and may be located in a jacket (12) having a gas inlet (24).

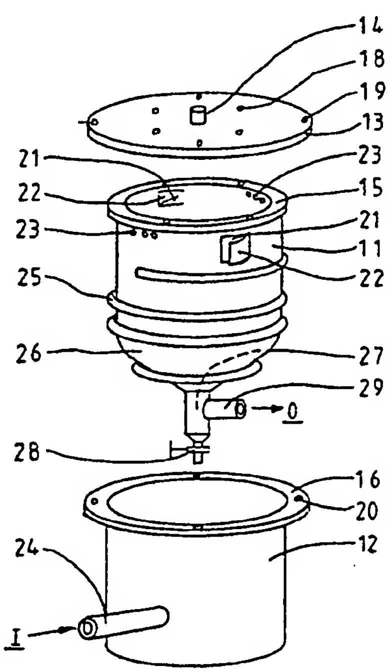

FIG 1

At least one drawing originally filed was informal and the print reproduced here is taken from a later filed formal copy.

The claims were filed later than the filing date within the period prescribed by Rule 25(1) of the Patents Rules 1982.

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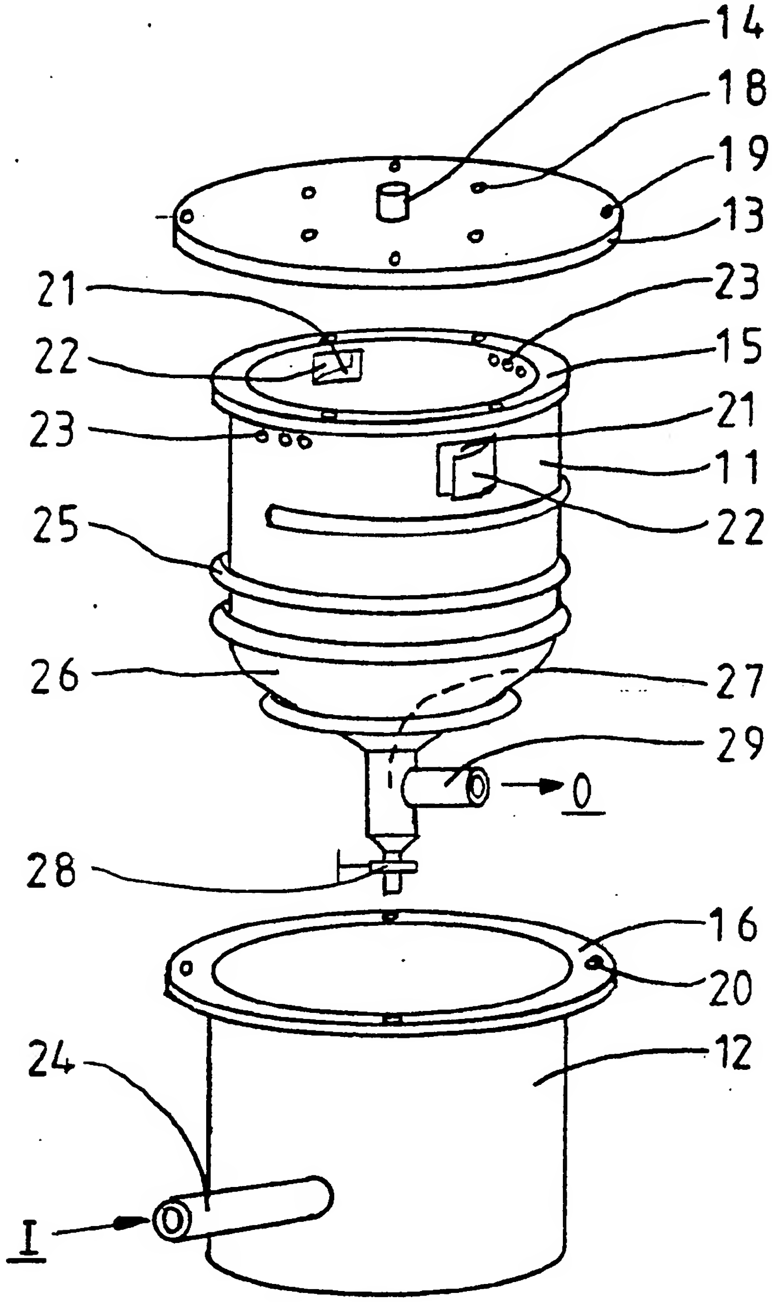

FIG 1

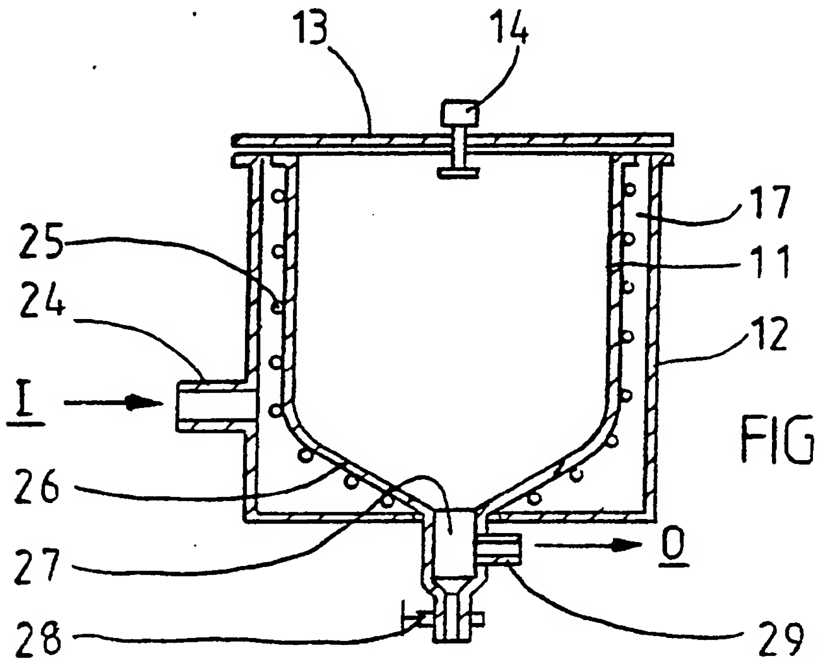

FIG 2

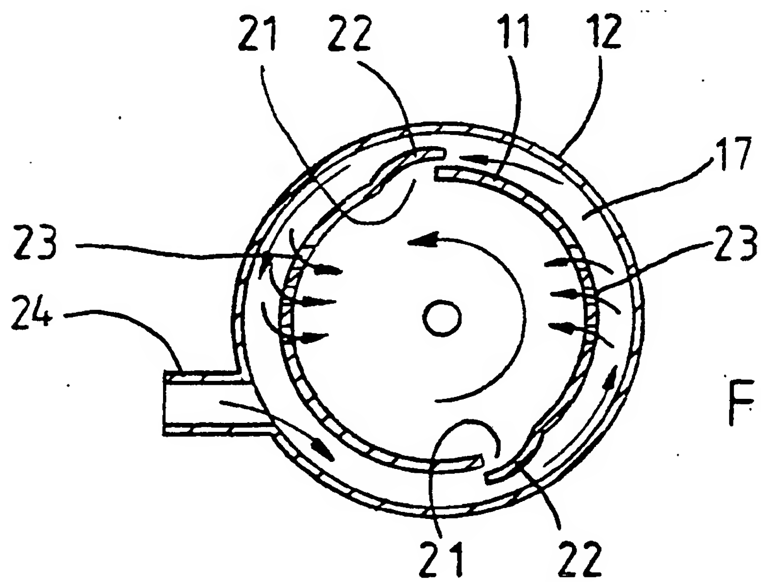

FIG 3

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Mixers

This invention relates to mixers, and concerns in particular the mixing of liquids into gases as may be required to produce a sterilizing medium for use in an isolator.

In many fields of technology there is a need for work to be carried out in an environment that is safely sealed off from the rest of the world. For example, in the biological sciences it is common to work with dangerously toxic or infectious materials (such as poisons, bacteria or viruses) and it will usually be desirable to carry out this work in a fully enclosed area from which the dangerous materials cannot easily escape into, and so contaminate, the surroundings. In the pharmaceutical and electronics industries, on the other hand, it may be desirable to work on some product (such as a drug or microchip) within a scrupulously clean enclosure, so as to prevent the ambient conditions contaminating the product.

Both of these situations require a volume of space to be sealed off - isolated - from its surroundings, and to meet this need technology has produced the isolator, which comes in sizes varying from that of a large (1x1x1 m, or about 2.5x2.5x2.5 ft) box up to that of a small room).

In essence, an isolator is little more than a sealed, bubble-like envelope in the wall of which is both a hatch (though which articles can be passed in and out) as well as means whereby the bubble's contents can b manipulated. The nvelope i natur lly made of some

(preferably transparent) material suitably resistant to whatever chemic ls and other substances are likely to come into contact with it both inside and outside the isolator (typical such materials are flexible polyvinyl chloride - PVC - film or sheet, but some isolators can be made of rigid materials such as a glass or PERSPEX (RTM)). One very successful form of isolator available today is a cuboidal "bubble" of flexible PVC suspended from an external framework that both shapes and supports the bubble, and a particular example of such an isolator is the subject of our co-pending Application for Letters Patent No: 88/05,817 ("Edgeseal"). The isolator there described has a two-part structure (instead of a one piece bubble), having a canopy, or upper tent-like part, similar to the conventional bubble envelope, and a base, or lower tray-like part, similar to the conventional trays for internal use, and the two are detachably sealed to each other around their respective perimeters to produce the isolator, the seal being secured by a special long but flexible clip-like device.

On occasion, it will be necessary to supply filtered air, or a sterilizing vapour, to the isolator. For example, isolators are frequently used in sterile applications such as the preparation of drugs for injection and parenteral nutrition, and in these cases the isolator, either empty or loaded with materials, must be rendered sterile prior to use. A variety of agents is available for this operation (common ones are 10% aqueous formaldehyde solution and 3.5% aqueous peracetic acid solution), and most are best presented to the isolator in the gas phase with a concentration around 5 to 10 gm/kg and a Relative Humidity (RH) of 90%. The invention proposes a novel form of mixer that should produce this vapour efficiently, safely and cheaply, so that isolat rs can be used in full-scale

pharmaceutical or similar production where these parameters are fundamental. More specifically, the invention suggests a novel way of evaporating the chosen sterilizing agent into and mixing it with an air stream to make a sterilizing vapour that can be passed through the isolator and its associated ventilation system to render them sterile.

Apparatus that evaporates and mixes the agent already exist, but it is very slow in operation since it produces only small volumes of vapour at low concentration. And whilst attempts have been made to speed up the process by recirculating the vapour, the resulting apparatus is complex, and hence large and very expensive. Moreover, previous sterilizers have also been both inconvenient and dangerous in that they have required a compressed air supply and heating of the sterilizing agent (percetic acid is explosive at concentrations above 50% and temperatures above 60°C).

The invention seeks to provide new mixing apparatus that fully vapourises a solution into an air flow in as small a volume as practicable and with minimum complexity.

In one aspect, therefore, the invention provides apparatus for mixing a vapourisable liquid into a gas, which apparatus comprises:-

an elongate mixing chamber having at one end an entry portal _via_ which gas may be fed into the chamber so as to swirl around and along the chamber to the other end, where there is an exit portal _via_ which the gas can leave the chamber; and

an atomiser to which can be fed the liquid to be mixed with the gas, which atomiser is so positioned in

the chamber relative to the entry portal that atomised liquid produc d thereby is drawn into and carried along with the swirling gas.

The apparatus of the invention is a mixer, and mixes a vapourisable liquid with a gas. The mixer may have many uses, but for application in the sterilizing field - especially in the sterilizing of isolators - the gas will generally be air, whilst the vapourisable liquid will be one of the present or proposed sterilizing liquids (such as the aqueous formaldehyde or aqueous peracetic acid solutions mentioned hereinbefore).

The mixer's main component is an elongate mixing chamber. Most preferably the chamber is cylindrical - the whole being of a barrel shape - and of a size suited to the flow rate of the gas passed therethrough. For an isolator of 1 m^3 (35 ft^3) in volume a sterilizing gas flow rate of from 10 to 30 m^3/hr (350 to 1050 ft^3/hr), preferably 25 m^3/hr (875 ft^3/hr) is generally used, and this can be achieved quite comfortably with a mixing barrel of around 0.6 m (2 ft) long and 0.16 m (0.5 ft) radius, giving a volume of about 0.05 m^3 (1.8 ft^3). Higher flow rates (for larger isolators, say) necessitate larger mixers, whilst lower rates can be achieved by smaller mixers. However, in order to promote good mixing and evaporation, with a reduced chance of atomised liquid droplets impinging upon the sides of the chamber, the volume of mixer employed is preferably attained using a wide and short chamber (like a barrel) rather than long and thin one (like a pipe).

At one end of the mixing chamber is an entry portal through which th gas can b fed so as to ttain a

swirling motion as it passes along and out of the chamber. Though it is possible to achieve the desired swirl in a number of ways - for instance, the gas could be fed in through the actual end wall of the chamber, and given a swirl by suitably placed baffles within the chamber - it is presently considered easiest and simplest to feed the gas in laterally - that is, from the side wall of the chamber generally towards the chamber's long axis somewhere between "radially" and "tangentially" (the chamber need not, of course, be of circular cross-section, but the use of these terms will explain the concept). Gas fed into the chamber in this manner swirls helically along around the axis, and out.

At the other end of the chamber (the end opposed to that where lies the entry portal) is an exit portal via which the gas, laden with vapour, can leave the chamber. This exit portal could be in the side wall of the chamber, but most conveniently (and to maintain the swirling conditions) it is in the end face - and, moreover, is generally axially aligned with the chamber. Furthermore, in order to ease the transition of the swirling gas from the relatively wide mixing chamber to and through the relatively narrow exit portal, this end face of the chamber is conveniently conical, narrowing outwards. Moreover, in order still further to ease the transition from the chamber to the exit portal, the conical end face is very preferably joined to the side wall by a gently curving portion rather than an abrupt angular change.

Positioned within the chamber and adjacent the entry portal is an atomiser, to which is fed the liquid to be mixed with the gas. This atomiser can be of any sort - a conventional pressure atomiser, of th am v riety as us d in scent sprays or aerosols, is quite

possible - but to allow the liquid to be fed thereto under minimum pressure (i.e., avoiding high pressure pumps) and yet to ensure atomisation it is preferred if the atomiser be an ultrasonic nebulising device, in which the liquid is fed (under low pressure) to an ultrasonically vibrating nozzle at which it is literally shaken into many microscopic drops of around 50 micrometer (0.002 in) diameter. A typical such atomiser is a Lechler US2 Model 100-061-16-30 available from Spraytech Ltd; its transducer can be supplied with an AC signal at from 30 to 60 KHz to atomise practically any liquid.

The atomiser is so positioned adjacent the chamber's entry portal that its output - the atomised liquid - is drawn into, mixed with, and carried along by, the incoming swirling gas. Though the atomiser could simply be in line with the incoming gas, and right next door to the entry portal, this is generally not preferred, for it may happen that the drops of atomised liquid, small though they be, are then simply blasted away onto the side of the chamber, where they coalesce to form a film of wasted, unvapourised liquid. Instead, then, it is preferred to position the atomiser some distance away from the entry portal, and out of the direct line of the input gas. Thus, supporting the atomiser from the end wall, and locating it axially of the chamber, meets both these requirements.

The flow rate of the input gas governs the flow rate of the sterilizing gas/vapour mixture leaving the mixer. The concentration of the sterilizing vapour in this mixture is determined by the rate at which sterilizer liquid is fed into the gas <u>via</u> the atomiser. Using a really efficient atomiser of the ultrasonic nebuliser variety the desired sterilizing vapour

concentration can be readily attain d by feeding in the liquid at as low a rate as from 1.5 to 4 ml minute (though the actual value is dependant on the ambient conditions).

It will normally be desirable, and perhaps even necessary, to heat the mixture of gas and liquid droplets both to promote rapid and full evaporation of the latter in the former and to allow for the heat energy used up (in the latent heat of evaporation) as the liquid vaporises. If the inner surface of the chamber is around the 35° to 55°C mark, especially about 40°C, that will usually be satisfactory. Accordingly, it will be advantageous both to heat the chamber and to heat the gas prior to feeding it in. Each of these ends can be achieved in any convenient way, but one in particular combines the two in an especially elegant fashion. Thus, the chamber is provided with a heating jacket the wall of which is spaced slightly from the wall of the mixing chamber, with heating coils, preferably electric, disposed in the intermural space (and preferably wrapped around the outside of the chamber itself) so as to heat both the chamber and the intermural volume between the jacket and chamber, and then the gas is fed to the chamber _via_ that intermural volume. In this way, the heating coils both pre-heat the gas and keep the swirling mixture hot.

Indeed, the use of a jacketted chamber gives rise to a particularly preferred embodiment of the invention, for the gas can be delivered "tangentially" into the intermural volume at that end corresponding to the _exit_ end of the chamber, can swirl around and along the intermural volume to the other end (that end corresponding to the _entry_ end of the chamber), and can there be directed, by baffles extending into the

intermural space, through the entry portal (or each such; in this preferred embodiment there are in fact two, diametrically arranged either side of the chamber) into the chamber, and then along and out as before. So efficient is this arrangement at inducing the desired swirl into the gas that it is, indeed, almost too powerful (and even at low flow rates may, as mentioned above, cause the liquid droplets to be flung directly to the chamber wall rather than being drawn into the gas stream). To avoid this possibility there are provided "spill holes" in the chamber entry portal end - conveniently two sets at the ends of a diameter crossing at right-angles that of the entry portal pair - where the incoming gas can "leak" prematurely, and with some local turbulence, into the chamber to reduce the very severe swirling that might otherwise be experienced.

The materials used for the mixer of the invention may be any convenient, provided of course that they can withstand the physical and chemical conditions involved. Thus, the mixing chamber itself is advantageously stainless steel (though certain plastics, or plastics- or ceramics-coated mild steel, aluminium or nickel might be satisfactory under some conditions, and indeed in a preferred embodiment the entry portal end of the chamber is a transparent plastics substance - PERSPEX, for example). And in the jacketted embodiment, the jacket can usually be a plastics material such as a rigid polyvinyl chloride (PVC) or a polyethylene.

An mbodiment of the invention is now described, though by way of illustration only, with reference to the accompanying diagrammatic Drawings in which

Figure 1 shows an "exploded" perspective view (from above) of a jacketted mixing device of the invention;

Figure 2 shows an axial section of the jacketted chamber of Figure 1; and

Figure 3 shows a trans-axial "section" of the jacketted chamber of Figure 1.

The mixer of the invention has three main parts, namely: a barrel-like cylindrical mixing chamber (generally 11); a correspondingly-shaped jacket (generally 12); and a circular lid (generally 13; this is the entry portal end of the chamber 11) with an atomiser (14) mounted centrally thereof. Both the chamber 11 and the jacket 12 have outwardly-directed flanges (respectively 15, 16) at their entry portal ends (the upper ends as viewed), and the chamber fits co-axially into the jacket (see Figures 2 and 3) leaving an annular intermural space (17) all around save where the flanges align flush. The lid 13 then fits on - in this embodiment it is bolted on (by bolts not shown passing through the relevant sets of apertures, as 18, 19, 20). More specifically, the chamber 11 is bolted to, and hangs from, the lid 13, whilst the lid is itself bolted to, and rests on, the jacket 12.

N ar the upper end of the chamber 11 is a pair of entry portals (as 21), disposed at the opposite ends of a diameter across the chamber. Each portal is a "square" aperture cut into the chamber wall, the section of wall then being folded out along one "vertical" edge to form a scoop or baffle (as 22) extending into the intermural space 17. And at each of the opposite ends of a diameter crossing the portal pair one at right-angles is a set of three "spill holes" (as 23).

Finally: at the base of the jacket 12 is a gas input pipe (24), through which gas can be blown "laterally" into the jacket at an angle halfway between "radial" and "tangential"; around the outer surface of the chamber side wall is wrapped an electric heating tape (25); and at the base (26) of the chamber 11 (which base is cone shaped, and is joined to the side walls by a gently curving portion) there is an exit portal (27) leading past a drain cock (28) to an output pipe (29).

The mixer of the Figures functions as follows:-

Air (I) is blown through the input pipe 24 into the intermural space 17 between the jacket 12 and the chamber 11. The orientation of this pipe 27 causes the air to circulate around the interspace 17 and move towards the top. As it rotates it picks up heat from the heating tape 25 (and from the outer surface of the chamber 11) before entering the chamber through the two entry portals 21. This arrangement serves two purposes: firstly, the air is pre-heated before entering the chamber 11; and secondly, the cold air coming in cools the jacket 12, so that no bulky thermal insulation is needed.

The scoops (or baffles) 22 are arranged to impart further vorticity to the air as it is deflected into the chamber 11, so that it takes a helical pathway (see Figure 3) towards the exit portal 27 in the centre of the coned base 26.

The nebulising ultrasonic atomiser 14 feeds sterilizing liquid into the chamber 11 as a mist of droplets with a median diameter of 50 micrometers. These are swiftly entrained in the helix of warm air, and evaporate completely before leaving the chamber. The temperature range for the inner surface of the chamber 11 is from 35° to 55°C, the preferred temperature being about 40°C.

The spill holes 23 are added to increase turbulence and hence mixing, and to prevent the mist droplets from being "centrifuged" onto the side wall of the chamber level with the nebuliser (if this does occur, them local cooling and condensation takes place, whereas what is needed is an even temperature).

Finally, the gas/sterilizer mixture leaves the chamber <u>via</u> the exit portal 27, and (at <u>Q</u>) leaves the apparatus through the output pipe 29.

With the abovementioned flow rates and temperatures, full and safe evaporation of the sterilizer liquid is achieved without the need for bulky compressors.

CLAIMS

1. Apparatus for mixing a vapourisable liquid into a gas, which apparatus comprises:-

an elongate mixing chamber having at one end an entry portal *via* which gas may be fed into the chamber so as to swirl around and along the chamber to the other end, where there is an exit portal *via* which the gas can leave the chamber; and

an atomiser to which can be fed the liquid to be mixed with the gas, which atomiser is so positioned in the chamber relative to the entry portal that atomised liquid produced thereby is drawn into and carried along with the swirling gas.

2. Mixing apparatus as claimed in Claim 1, wherein the elongate mixing chamber is cylindrical, the whole being of a barrel shape.

3. Mixing apparatus as claimed in Claim 2, wherein the cylindrical mixing barrel is 0.6 m (2 ft) long and 0.16 m (0.5 ft) radius.

4. Mixing apparatus as claimed in any of the preceding Claims, wherein the entry portal is disposed to feed the gas in laterally - that is, from the side wall of the chamber generally towards the chamber's long axis somewhere between "radially" and "tangentially".

5. Mixing apparatus as claimed in any of the preceding Claims, wherein the exit portal is in the end face, and is generally axially aligned with the chamber.

6. Mixing apparatus as claimed in Claim 5, wherein this end face of the chamber is conical, narrowing outwards.

7. Mixing apparatus as claimed in any of the preceding Claims, wherein the atomiser is an ultrasonic nebulising device.

8. Mixing apparatus as claimed in any of the preceding Claims, wherein the atomiser is positioned some distance away from the entry portal, and out of the direct line of the input gas.

9. Mixing apparatus as claimed in Claim 8, wherein the atomiser is supported from the end wall, and located axially of the chamber.

10. Mixing apparatus as claimed in any of the preceding Claims, wherein the mixing chamber is provided with a heating jacket the wall of which is spaced slightly from the wall of the mixing chamber, with heating coils disposed in the intermural space, around the outside of the chamber itself, so as to heat both the chamber and the intermural volume between the jacket and chamber, and then the gas is fed to the chamber via that intermural volume.

11. Mixing apparatus as claimed in Claim 10, wherein gas delivered "tangentially" into the intermural volume at that end corresponding to the exit end of the chamber swirls around and along the intermural volume to the other end (that end corresponding to the entry end of the chamber), and is there directed, by baffles extending into the intermural space, through the or each entry portal into the chamber.

12. Mixing apparatus as claimed in any of the preceding Claims and substantially as described hereinbefore

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